REMARKS

Applicant acknowledges receipt of the Office Action mailed December 30, 2003.

As explained below, Applicant submits that the amendment to Claim 105 is sufficient to overcome both of the outstanding rejections.

Written description support for the amendment of Claim 105 can be found in the Specification as originally filed. More specifically, the Specification describes on page 20 at line 15, and on page 22 at line 18, the use of shared sets of primers for co-amplifying the pseudo target and the analyte polynucleotide. The working Examples also describe this configuration, and so further support the amendment.

Claims 105-106, 108-110 and 116 remain pending following entry of this Amendment.

Entry of this Response is respectfully requested.

The Rejection Under § 102(e)

Claims 105-106, 108 and 116 have been rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,952,202 ("**Aoyagi**") which discloses co-amplification and detection of a target polynucleotide and an internal control polynucleotide ("ICP") in a real-time format. According to the cited reference, the two amplicon species are synthesized using different primer sets and are detected using different self-reporting probes. The rejection cited Example 5 as instructing that signals representing the detection of target and internal control polynucleotides could be detected as a "Ct value" which represents a threshold value for determining the presence or absence of DNA in a test sample. Although the rejection refers to col. 36, lines 1-26 of the

prior art citation, Applicant believes this reference is in error because the Aoyagi patent does not contain col. 36.

The instantly amended claims do not embrace the method of **Aoyagi** because the claimed method specifies nonobvious limitations that are not described in the cited reference. More particularly, amended Claim 105 specifies that the pseudo target and the analyte polynucleotide are co-amplified using the same set of two oligonucleotide primers. **Aoygai** specifically guides away from the use of a shared primer set in under the first full paragraph of column 6, where it is stated (col. 6 at line 11):

> ***A pervasive difficulty is keeping amplification of the control polynucleotide from interfering with target amplification or detection of the product.*** Internal control polynucleotides (ICP) undergo amplification within the same reaction chamber as the known or unknown target polynucleotide, imparting convenience in preparing samples and measuring results. The ICP may be endogenous, i.e. from the same source, genome, chromosome, gene, plasmid, or fragment as the target. Endogenous ICP are subject to amplification inhibitors and can therefore give a false negative signal. Endogenous ICP also may have priming sites for target primers and therefore give a false positive signal. ***In fact, endogenous ICP systems may share one or more primers with the target. Exhaustion of shared primers leads to inaccurate PCR quantitation and limited dynamic range. Another negative feature of endogenous ICP*** is the necessity to select, design, and purify ICP, ICP primers, and ICP self-quenching probe for each target to ensure compatibility and viable amplification. A universal exogenous ICP which is not derived from the same source, etc. as the target is therefore desirable, to avoid these disadvantages. [***Emphasis added***]

That which **Aoyagi** counsels against (i.e., interference with target amplification) is precisely an object of the present invention which employs pseudo targets to control the magnitude of target analyte amplicon production. While **Aoyagi** describes problems that result from the use of shared

primers, Applicant showed how shared primers can be used to advantage. Thus, the present invention differs fundamentally from that described by **Aoygai**, and the instant amendments distinguish the different inventions.

Since the instant claims do not embrace the method of **Aoyagi** by virtue of incorporating the limitations of amended Claim 105, **Aoygai** cannot anticipate the claims. Moreover, **Aoyagi** actually teaches away from the use of shared primers for amplifying the analyte and a second polynucleotide which the rejection asserts to fall within the scope of a pseudo target. Accordingly, withdrawal of the rejection of Claims 105-106, 108 and 116 under 35 U.S.C. § 102(e) is appropriate.

The Rejection Under § 103

Aoyagi et al., and Jurriaans et al.

Claims 109 and 110 have been rejected under 35 U.S.C. § 103(a) as *prima facie* obvious over the disclosure of the **Aoyagi** patent in view of a scientific journal article by Jurriaans et al., ("**Jurriaans**"). The rejection essentially states that, because **Aoyagi** discloses methods of amplifying an internal control polynucleotide, and because **Jurriaans** describes determining the amounts of HIV-1 RNA and DNA in clinical samples by nucleic acid amplification in a method of monitoring disease progression, it would have been obvious to use the method of **Aoyagi** for the detection of HIV-1 nucleic acids in accordance with **Jurriaans**. According to the rejection, one of ordinary skill in the art would have been motivated to use real-time nucleic acid amplification with internal controls to result in a rapid and accurate assay.

Claims 109 and 110 incorporate the nonobvious limitations recited in amended Claim 105, and so also are nonobvious. Amended Claim 105 requires that the pseudo target and the analyte

polynucleotide are co-amplified using the same set of two oligonucleotide primers, a feature of the invention which actually goes opposite guidance which appears in the **Aoygai** patent, and which is discussed above. **Jurriaans** says nothing to suggest that it would be a good idea to co-amplify the ICP of **Aoyagi** and a viral analyte, such as an HIV-1 polynucleotide, using a shared set of two primers which **Aoyagi** guides against.

Since all of the claims require the use of a shared set of two primers for co-amplifying the pseudo target and the analyte polynucleotide, since the prior art actually leads away from the use of shared primers because of alleged undesirable interference with target amplification and quantitation, and since Applicant proceeded opposite the teaching of the prior art to create the instant invention, the claims cannot be considered obvious in light of the prior art. Accordingly, withdrawal of the rejection under 35 U.S.C § 103 in light of **Aoygai** in view of **Jurriaans** is respectfully requested.

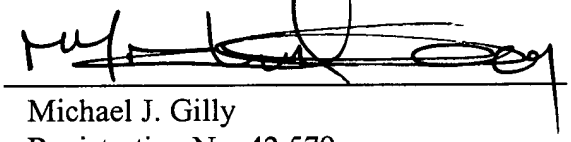
CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the telephone number shown below.

Respectfully submitted,

GEN-PROBE INCORPORATED

Dated: May 27, 2004

By: 

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